REMARKS

Claim Amendments

Claim 110 has been canceled, Claims 16, 21, 27, 34, 41, 47, 53, 60, 84, 103 and 115 have been amended and new Claims 116-121 have been added.

Claims 27 and 103 have been amended to correct informalities.

Claims 16, 21, 34, 41, 47, 53, 60, 84 and 115 have been amended to recite "a mammalian ligand." Support for this recitation is found, for example, at page 31, lines 3-6.

New Claims 116, 117, 118, 119, 120 and 121 are modeled after independent Claims 21, 34, 41, 25, 26 and 84 respectively, but recite "a chemokine ligand." Support for this recitation is found, for example, at page 14, lines 9-12 and page 18, lines 25-27.

Therefore, the amended and new claims are supported by the subject application as originally filed and this Amendment adds no new matter.

Additional remarks addressing the Examiner's comments and rejections are set forth below with reference to the numbered paragraphs of the Office Action.

Paragraph 2. Anticipated Rejoinder of Claims Pursuant to M.P.E.P. § 821.04

Applicants thank the Examiner for her acknowledgment of the request for rejoinder of Claims 16, 47, 53, 60 and 115. Withdrawn independent process Claims 16, 47, 53, 60 and 115 have been amended in a manner analogous to independent product Claim 21. Therefore, in accordance with M.P.E.P. § 821.04, Claims 16, 47, 53, 60 and 115 should be rejoined and allowed upon allowance of Claim 21.

Paragraph 3. Information Disclosure Statement and Request for Acknowledgment of Consideration of Supplemental Information Disclosure Statement

Applicants thank the Examiner for her acknowledgment of consideration of the references cited in the Information Disclosure Statement filed on August 27, 2001. Applicants respectfully request that the Examiner consider and acknowledge the references cited in the Supplemental Information Disclosure Statement filed on August 25, 2003.

Paragraphs 5 and 6. Specification

The title on pages 1 and 87 has been amended to delete the word "novel." In addition, the abstract has been amended to be less than 150 words, in compliance with M.P.E.P. § 608.01(b).

Paragraph 8. Priority

The RELATED APPLICATIONS paragraph on page 1 has been amended to indicate that U.S. Application No. 09/449,437 has issued as U.S. Patent No. 6,319,675 B1.

Paragraphs 9 and 10. Claim Objections

Claims 27 and 110 are objected to under 37 C.F.R. § 1.75 as being substantial duplicates of one another. The Examiner states that although Claim 27 recites that the binding is to Bonzo and Claim 110 recites that the binding is to mammalian Bonzo, both claims depend from Claim 21, which recites mammalian Bonzo. Claim 110 has been canceled, thereby obviating this objection.

The Examiner has further objected to Claim 27 because it appears that a semicolon, rather than a comma, is needed following recitation of ATCC Accession No. PTA-991 and ATCC Accession No. PTA-992. Claims 27 and 103 have been amended to insert appropriate punctuation, as suggested by the Examiner.

Paragraph 12. Rejection of Claims 23, 39 and 46 under 35 U.S.C. § 112, second paragraph

Claims 23, 39 and 46 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicants regard as the invention. Specifically, the Examiner states that Claims 23, 39 and 46 are indefinite in that they describe the product of interest by an arbitrary protein name, i.e., SExCkine, and that the instant recitation fails to distinctly claim the nature of this protein. (Office Action, page 3, lines 18-20).

The second paragraph of 35 U.S.C. § 112 requires only that the claims "set out and circumscribe a particular area with a reasonable degree of precision and particularity." In re Moore and Janoski, 169 USPQ 236, 238 (CCPA 1971). Further, the meaning of the claims is not analyzed in a vacuum, but in light of the teachings of the prior art and of the specification as it

would be interpreted by one possessing the ordinary level of skill in the pertinent art. Id. at 238. In addition, M.P.E.P. §2111.01 and §2173.01 state that "applicants are their own lexicographers" and that they can define the claims in "whatever terms they choose so long as the terms are not used in ways contrary to accepted meaning in the art." M.P.E.P. § 2111.01, p. 2100-48, and §2173.01, p. 2100-198 (8th Ed., Feb., 2003).

In contrast to the Examiner's assertion, the term "SExCkine" is clearly described in Applicants' specification. For example, Applicants' specification teaches that the chemokine ligand SExCkine (Spleen Extracted Chemokine), which binds and activates Bonzo, is also referred to as chemokine alpha-5, as taught by WO 99/27078, published on June 3, 1999 (Reference AM, of record). (Specification, page 3, lines 19-22 and page 14, lines 9-12). Applicants teach the nucleic acid sequence of a cDNA encoding human SExCkine (SEQ ID NO:3) and the amino acid sequence of the encoded human SExCkine polypeptide (SEQ ID NO:4). Specification, page 7, lined 11-19 and Figure 3. Applicants also disclose the nucleic acid sequence of a cDNA encoding human chemokine alpha-5 (SEQ ID NO:5) and its encoded amino acid sequence, as taught by WO 99/27078. (Specification, page 7, lines 20-23 and Figure 4A-4C).

In addition, Applicants teach:

> As used herein "mammalian SExCkine" refers to naturally-occurring or endogenous mammalian SExCkine proteins (e.g., SEQ ID NO:4, SEQ ID NO:6) and to proteins having an amino acid sequence which is the same as that of a naturally-occurring or endogenous corresponding mammalian SExCkine protein (e.g., recombinant proteins, synthetic proteins (i.e., produced using the methods of synthetic organic chemistry)). Accordingly, as defined herein, the term includes mature protein, polymorphic or allelic variants, and other isoforms of a mammalian SExCkine (e.g., produced by alternative splicing, proteolytic processing or other cellular processes), and modified or unmodified forms of the foregoing (e.g., lipidated, glycosylated (e.g., with glycosaminoglycans), unglycosylated,). Naturally-occurring or endogenous mammalian SExCkine proteins include wild type proteins such as transmembrane SExCkine and soluble SExCkine, polymorphic or allelic variants and other isoforms which occur naturally in mammals (e.g., humans, non-human primates). Such proteins can be recovered or isolated from a source which naturally produces mammalian SExCkine, for example. These proteins and mammalian SExCkine proteins having the same amino acid sequence as a naturally-occurring or endogenous corresponding mammalian SExCkine, are referred to by the name of the corresponding mammal. For example, where the corresponding mammal is a

> human, the protein is designated as a human SExCkine protein (e.g., a recombinant human SExCkine produced in a suitable host cell).

Specification, page 19, lines 3-22.

Therefore, Applicants' specification clearly conveys what is meant by the recitation "SExCkine." In view of the detailed teachings of the specification and the standard for analyzing claimed subject matter as set out in Moore and Janoski, it is clear that the person of ordinary skill in the art would understand the invention of Claims 23, 39 and 46, and that these claims meet the requirement of 35 U.S.C. § 112, second paragraph. Reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 15. Rejection of Claims 21, 22, 24-27, 34-38, 40-45, 84, 88 and 97-114 under 35 U.S.C. § 112, first paragraph

Claims 21, 22, 24-27, 34-38, 40-45, 84, 88 and 97-114 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner states that independent Claims 21, 34 and 41, and claims dependent therefrom, which recite an antibody or a cell line producing an antibody, wherein the antibody inhibits the binding of a ligand to Bonzo, or a cellular response to binding of a ligand, are not supported by an adequate written description in the specification. According to the Examiner, the specification lacks adequate written description for the genus of molecules that are "ligands that bind Bonzo."

Applicants disagree that the specification lacks adequate written description to support a genus of molecules that are "ligands that bind Bonzo." However, in order to expedite prosecution, independent Claims 21, 31, 34, 41 and 84 have been amended to recite "mammalian ligand." Applicants disclose nucleic acid and amino acid sequences for several mammalian ligands that bind Bonzo including, e.g., human SExCkine (SEQ ID NOs:3 and 4; Figure 3), human chemokine alpha-5 (SEQ ID NOs:5 and 6; Figures 4A-4C) and human platelet factor-4 (SEQ ID NOs:7 and 8; Figures 5 and 6). Thus, the detailed teachings of the specification provide adequate written description for a genus of "mammalian ligands that bind Bonzo." Reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 18. Rejection of Claims 21-27, 34-36 and 103-114 under 35 U.S.C. § 102(a)

Claims 21-27, 34-46 and 103-114 are rejected under 35 U.S.C. § 102(a) as being anticipated by Catalog #MAB699 (STRL 33/Bonzo Monoclonal antibody, *de novo*, New Products from R & D Systems, page 7 (April 1999); cited as Reference AY4), as evidenced by the monoclonal anti-human STRL 33/Bonzo Antibody Technical Information (R&D Systems, Inc. (May 10, 1999); cited as Reference AZ4) and the instant specification (Figure 32 and its legend at page 13, lines 12-18).

The Examiner states that Catalog #MAB699 teaches a monoclonal antibody that binds human Bonzo. (Office Action, page 6, line 6). The Examiner further states that the monoclonal anti-human STRL 33/Bonzo Antibody Technical Information sheet (Reference AZ4) provides evidence that both a monoclonal antibody that binds human Bonzo and hybridoma 56811.111, which produces this monoclonal antibody, were known or used and described in a printed publication in this country, before the invention thereof by Applicant. (Office Action, page 6, lines 6-10). The Examiner states that Catalog #MAB699 and the Technical Information sheet do not teach any functional properties of this antibody but that Figure 32 of Applicants' specification shows that MAB699 inhibits SExCkine-induced chemotaxis of Bonzo/L1.2 cells. (Office Action, page 6, lines 11-14). According to the Examiner, the instantly recited properties of inhibition of SExCkine binding and inhibition of signal transduction or various other cellular responses, such as calcium flux, would be inherent properties of MAB699. (Office Action, page 6, lines 16-19). Therefore, the Examiner is of the opinion that Catalog #MAB699 anticipates the instant claimed invention.

Catalog #MAB699 (STRL 33/Bonzo Monoclonal antibody, *de novo*, New Products from R & D Systems) bears the date of April, 1999. The evidence presented in the Declaration Under 37 C.F.R. § 1.131, filed concurrently herewith, establishes that Applicants were in possession of several monoclonal antibodies that bind Bonzo, including mAb 4A11, mAb 4F7, mAb 7A2, mAb 7F3, mAb9G2 and mAb10E3, prior to March 24, 1999. The Declaration Under 37 C.F.R. § 1.131 further establishes that Applicants were in possession of cells producing monoclonal antibodies that bind Bonzo prior to March 24, 1999. As disclosed in the specification, mAb 4A11, mAb 7A2, mAb 7F3 and mAb 9G2 inhibit binding of SExCkine to Bonzo (Specification, page 62, Table 1, page 70, lines 24-26 and Figure 31). Applicants' specification further teaches

that mAb 7F3 inhibited SExCkine-induced chemotaxis of cytokine-induced killer (CIK) cells (Specification, page 71, lines 7-12 and Figure 21) and *in vitro* derived TH2 lymphocytes (Specification, page 71, lines 15-20 and Figure 28), both of which express Bonzo. Therefore, the evidence presented in the Declaration Under 37 C.F.R. § 1.131 establishes that Applicants were in possession of several antibodies and isolated cells that are encompassed by the rejected claims prior to publication of Catalog #MAB699. Consequently, Catalog #MAB699 cannot be relied upon in a rejection under 35 U.S.C. § 102(a). Reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 19. Rejection of Claims 21, 22, 24-27, 34-38, 40-45, 97-102 and 109-114 under 35 U.S.C. § 102(a)

Claims 21, 22, 24-27, 34-38, 40-45, 97-102 and 109-114 are rejected under 35 U.S.C. § 102(a) as being anticipated by MacPhee *et al.* (WO 99/50670; cited as Reference AL). The Examiner states that MacPhee *et al.* teach that platelet factor 4 (PF-4) binds to a PF-4 receptor that is the same as human Bonzo. (Office Action, page 7, lines 3-4). The Examiner further states that MacPhee *et al.* teach that binding of the ligand PF-4 to the cell surface PF-4 receptor/Bonzo results in cellular responses including chemotaxis, calcium flux, and the tranduction of various other signals in to the cell, and that assays that detect these signals can be used to identify inhibitors. (Office Action, page 7, lines 4-8). The Examiner states that MacPhee *et al.* teach antibodies that can be produced that neutralize receptor function as well as cell lines that produce such antibodies. (Office Action, page 7, lines 9-10). According to the Examiner, the claimed functional limitations would be inherent properties of an antibody that bound human Bonzo and neutralized binding of PF-4. (Office Action, page 7, lines 12-13). Therefore, the Examiner is of the opinion that MacPhee *et al.* anticipates the instant claimed invention.

WO 99/50670 (MacPhee *et al.*) has an effective date of October 7, 1999, its international publication date. As described above (see text under Paragraph 18), the evidence presented in the Declaration Under 37 C.F.R. § 1.131, filed concurrently herewith establishes that Applicants were in possession of several antibodies and isolated cells that are encompassed by the rejected claims prior to March 24, 1999. Therefore, the disclosure of WO 99/50670 (MacPhee *et al.*)

cannot be relied upon in a rejection under 35 U.S.C. § 102(a). Reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 20. Rejection of Claims 21, 22, 34, 38 and 40 under 35 U.S.C. § 102(b)

Claims 21-22, 34, 38 and 40 are rejected under 35 U.S.C. § 102(b) as being anticipated by Farber *et al.* (WO 98/44098, cited as Reference AP). Specifically, the Examiner states that Farber *et al.* teach that the human STRL33 protein is bound by HIV as part of the entry of HIV into cells, and therefore HIV is a ligand of human STRL33. The Examiner further states that Farber *et al.* teach antibodies and antibody fragments that bind STRL33 and block membrane fusion between HIV and a target cell, as well as cell lines and hybridomas.

While Applicants disagree that Farber *et al.* anticipates the claimed invention, independent Claims 21 and 34 have been amended to recite "mammalian ligand", thereby obviating this rejection.

Paragraph 22. Rejection of Claims 84 and 88 under 35 U.S.C. § 103(a)

Claims 84 and 88 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Catalog #MAB699 (STRL 33/Bonzo Monoclonal antibody, *de novo*, New Products from R & D Systems, page 7 (April 1999); cited as Reference AY4), as evidenced by the monoclonal anti-human STRL 33/Bonzo Antibody Technical Information (R&D Systems, Inc. (May 10, 1999); cited as Reference AZ4) and the instant specification (Figure 32 and its legend at page 13, lines 12-18), in view of Jardieu *et al.* (U.S. Patent No. 6,037,454).

The Examiner states that the claims are drawn to a test kit for detecting the presence of Bonzo in a biological sample, wherein the test kit comprises an antibody that binds Bonzo and inhibits binding of a ligand, and one or more ancillary reagents suitable for binding the antibody-Bonzo complex. (Office Action, page 8, lines 19-22). According to the Examiner, the formulation of antibodies that detect receptors expressed on the surface of a cell into a kit comprising ancillary reagents for the detection of antibody-receptor complex would have been obvious to the ordinary skilled artisan at the time the invention was made in view of any teaching of the antibody, but particularly in view of a teaching to use the antibody in a detection assay. (Office Action, page 8, lines 28-32). The Examiner further states that Jardieu *et al.* teach: (i)

antibodies to another cell surface receptor, CD11A; (ii) that such antibodies can be used in numerous diagnostic assays to detect proteins; and (iii) that antibodies and ancillary agents for detecting binding of the antibody to the target antigen may be packaged together in a kit. (Office Action, page 8, lines 32-37). Therefore, in the Examiner's view, it would have been obvious to the ordinary artisan at the time the invention was made to combine MAB699 with one or more ancillary agents for detecting the antibody in complex with Bonzo. (Office Action, page 9, lines 1-2). The Examiner states that the ordinary artisan would have been motivated to provide the antibody in a kit as a matter of convenience, as taught by Jardieu *et al.* (Office Action, page 9, lines 3-4). The Examiner further states that in view of the teachings of MAB699 and its applicability in detection assays, and the teachings of Jardieu *et al.* regarding the numerous ancillary reagents available, the ordinary artisan would have had a reasonable expectation of formulating the antibody in a kit with one or more ancillary reagents. (Office Action, page 9, lines 4-7). Therefore, according to the Examiner, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary. (Office Action, page 9, lines 7-9).

As described above (see text under Paragraph 18), the evidence presented in the Declaration Under 37 C.F.R. § 1.131 establishes that Applicants were in possession of several antibodies and isolated cells that are encompassed by the rejected claims prior to March 24, 1999. Therefore, the disclosure of Catalog #MAB699, which was published in April, 1999, cannot be relied upon in a rejection under 35 U.S.C. § 103(a). Reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 23. Rejection of Claim 84 under 35 U.S.C. § 103(a)

Claim 84 is rejected under 35 U.S.C. § 103(a) as being unpatentable over MacPhee *et al.* (WO 99/50670, cited as Reference AL). The Examiner states that although MacPhee *et al.* do not teach an antibody to PF4 receptor/Bonzo in a test kit comprising one or more ancillary reagents suitable for detecting an antibody-Bonzo complex, that the formulation of a kit comprising antibodies that detect a cell-surface receptor and ancillary agents for detecting antibody-receptor complex would have been obvious to the ordinary artisan at the time of the

invention. (Office Action, page 9, lines 16-20). According to the Examiner, it would have been obvious to the ordinary artisan at the time the invention was made to combine the anti-PF4 receptor/Bonzo antibody taught by MacPhee *et al.* with one or more ancillary for detecting the antibody in complex with Bonzo. (Office Action, page 9, lines 27-29). The Examiner states that the ordinary artisan at the time the invention was made would have been motivated to provide the antibody in a kit as a matter of convenience, as taught by Jardieu *et al.* (Office Action, page 9, lines 29-31). The Examiner further states that in view of the teachings of MacPhee *et al.* of the anti-PF4 receptor/Bonzo antibody, and the teachings of Jardieu *et al.* regarding the numerous ancillary reagents available, the ordinary artisan would have had a reasonable expectation of formulating the antibody in a kit with one or more ancillary reagents. (Office Action, page 9, lines 31-33). Therefore, according to the Examiner, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary. (Office Action, page 9, lines 34-36).

As described above (see text under Paragraph 19), the evidence presented in the Declaration Under 37 C.F.R. § 1.131 establishes that Applicants were in possession of several antibodies and isolated cells that are encompassed by the rejected claims prior to March 24, 1999. MacPhee *et al.* (WO 99/50670) has an effective date of October 7, 1999, its international publication date. Therefore, the disclosure of MacPhee *et al.* cannot be relied upon in a rejection under 35 U.S.C. § 103(a). Reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 25. Provisional Rejection of Claims 21 and 34 under 35 U.S.C. § 101

The Examiner has provisionally rejected Claims 21 and 34 under 35 U.S.C. § 101 as claiming the same invention as that of Claims 21 and 34 of copending U.S. Application No. 10/174,293 (Attorney Docket No. 1855.1070-006).

Claims 21 and 34 as amended are no longer claiming the same invention as Claims 21 and 34 of copending U.S. Application No. 10/174,293 (Attorney Docket No. 1855.1070-006). In addition, as stated by the Examiner, this is a provisional double patenting rejection because the claims deemed to be conflicting have not yet been patented. If this provisional rejection is the

only rejection remaining after entry and consideration of this Amendment, Applicants respectfully request that the Examiner withdraw the rejection and permit the subject application to issue as a patent, in accordance with U.S. Patent Office procedure (see, M.P.E.P. § 804(I)(B), p. 800-19, (8th Ed., Latest Rev., 2003)).

Paragraph 27. Provisional Rejection of Claims 21-46, 84, 88 and 97-114 under the Judicially Created Doctrine of Obviousness-Type Double Patenting

The Examiner has provisionally rejected Claims 21-46, 84, 88 and 97-114 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 21, 28, 31, 34, 90, 197-201, 203, 205 and 206 of copending U.S. Application No. 10/174,293 (Attorney Docket No. 1855.1070-006). The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because the antibodies, cells producing the antibodies and kits comprising the antibodies are either the same species as recited in the instant claims, are species that anticipate the instantly claimed genus of antibodies and cells, or recite a genus in which an instantly claimed species is an obvious embodiment.

As stated by the Examiner, this is a provisional obviousness-type double patenting rejection because the claims deemed to be conflicting have not yet been patented. If this provisional rejection is the only rejection remaining after entry and consideration of this Amendment, Applicants respectfully request that the Examiner withdraw the rejection and permit the subject application to issue as a patent, in accordance with U.S. Patent Office procedure (see, M.P.E.P. § 804(I)(B), p. 800-19, (8th Ed., Latest Rev., 2003)).

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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